13, 2002 accompanies this response.

AMENDMENT

In the specification: Please amend the specification as follows (also enclosed is a mark-up under Rule 121).

On page1, line 23, to page 2, line 5, please replace with the following paragraph:

The second member of the ErbB family, p185^{neu}, was originally identified as the product of the transforming gene form neuroblastomas of chemically treated rats. The activated form of the *neu* proto-oncogene results from a point mutation (valine to glutamic acid) in the transmembrane region of the encoded protein. Amplification of the human homolog of *neu* is observed in breast and ovarian cancers and correlates with a poor prognosis (Slamon *et al.*, *Science*, 235:177-82(1997); Slamon *et al.*, *Science*, 244:707-712 (1989); and U.S. Pat. No. 4,968,603). To date, no point mutation analogous to that in the *neu* proto-oncogene has been reported for human tumors. Overexpression of ErbB2 (frequently but not uniformly due to gene amplification) has also been observed in other carcinomas including carcinomas of the stomach, endometrium, salivary gland, lung, kidney, colon, thyroid, pancreas and bladder. See, among others, King *et al.*, *Science*, 229:974 (1985); Yokota *et al.*, Lancet, 1:765-767 (1986); Fukushige *et al.*, *Mol. Cell Biol.*, 6:955-58 (1986); Guerin *et al.*, *Oncogene Res.*, 3:21-31 (1988); Cohen *et al.*, *Oncogene*, 4:81-88 (1989); Yonemura *et al.*, *Cancer Res.*, 51:1034 (1991); Borst *et al.*, *Gynecol. Oncol.*, 38:364 (1990); Weiner *et al.*, *Cancer Res.*, 50:421-25 (1990); Kern *et al.*, *Cancer Res.*, 50:5184 (1990); Park *et al.*, *Cancer Res.*, 49:6605 (1989); Zhau *et al.*, *Mol. Carcinog.*, 3:254-257 (1990); Aasland *et al.*, *Br. J. Cancer,*

57:358-363 (1988); Williams *et al.*, *Pathiobiology*, 59:46-52 (1991); and McCann *et al.*, *Cancer*, 65:88-92 (1990). ErbB2 may be overexpressed in prostate cancer (Gu *et al.*, *Cancer Lett.*, 99:185-189 (1996); Ross *et al.*, *Hum. Pathol.*, 28:827-833 (1997); Ross et al., *Cancer*, 79:2162-2170 (1997); and Sadasivan *et al.*, *J. Urol.*, 150:126-131 (1993)). Antibodies directed against the rat $p185^{neu}$ and human ErbB2 protein products have been described. Drebin and his colleagues have raised antibodies against the rat *neu* gene product, $p185^{neu}$. See, for example, Drebin *et al.*, *Cell*, 41:695-706 (1985); Myers *et al.*, *Meth. Enzym.*, 198: 277-290 (1991); and WO94/22478. Drebin *et al.*, *Oncogene*, 2:273-277 (1988) report that mixtures of antibodies reactive with two distinct regions of $p185^{neu}$ result in synergistic anti-tumor effects on *neu*-transformed NIH-3T3 cells implanted into nude mice. See also U.S. Patent 5,824,311, issued October 20, 1988.

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On page 43, lines 5-14, please replace with the following paragraph:

The murine monoclonal antibodies 2C4, 7F3, and 4D5 which specifically bind the extracellular domain of ErbB2 were produced as described in Fendly *et al.*, *Cancer Research*, 50:1550-1558 (1990). Briefly, NIH 3T3/HER2-3_{400} cells (expressing approximately 1 x 10^5 ErbB2 molecules/cell) produced as described in Hudziak *et al.*, *Proc. Natl. Acad. Sci (USA)*, 84:7159-7163 (1987) were harvested with phosphate buffered saline (PBS) containing 25 mM EDTA and used to immunize BALB/c mice. The mice were given injections IP of 10^7 cells in 0.5 ml PBS on weeks 0, 2, 5, and 7. The mice with antisera that immunoprecipitated ^{32}P-labeled ErbB2 were given i.p. injections of a wheat gem agglutinin-Sepharose (WGA) purified ErbB2 membrane extract on weeks 9 and 13. This was followed by an i.v. injection of 0.1 ml of the ErbB2 preparation and the splenocytes were fused with mouse myeloma line X63-Ag8.653. Hybridoma supernatants were

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